REMARKS

Claims 25-50, 60-124, 126-131, 133-150, and 154-155 will be pending in this application upon entry of the present response. Claims 125, 151-153 have been canceled without prejudice or disclaimer. Applicants hereby retain the right to pursue said canceled subject matter in continuing applications.

Applicants note that new claims 152-155 were added in an amendment submitted on November 21, 2001. However, the Patent Office did not acknowledge these newly added claims on the Office Action Summary cover sheet (*see* Paper No. 22, mailed April 22, 2002). Applicants however, failed to bring this to the Patent Office's attention earlier. The error in not doing so is regretted and Applicants kindly request acknowledgement of these claims.

The various claim amendments are fully supported by the specification, claims, drawings, and sequence listing as originally filed, and thus no new matter has been added.

I. Examiner Interview Summary

Applicants thank the Examiner and SPE Eyler for the interview conducted on February 5, 2003. During the interview, it was indicated that the enablement rejection of claims directed to polypeptides comprising fragments of SEQ ID NO:2 in Paper No. 26 would be withdrawn if the claims were amended to recite "consisting of" instead of "comprising". *See* Interview Summary, Paper No. 28.

The Examiner and Applicants' representatives also discussed potential amendments of claims directed to variants of SEQ ID NO:2. *See* Interview Summary, Paper No. 28. It was suggested during the interview that Applicants should request reconsideration by the Examiner of the three previously submitted Declarations under 37 C.F.R. §1.132 and of the arguments of record in which use of the instant invention for either enhancing or inhibiting immune cell proliferation is supported.

As a result of the interview Applicants have prepared this amendment and response in accordance with the issues discussed during the Examiner Interview, set forth below.

II. Rejections under 35 U.S.C. §112, first paragraph- Enablement

Claims 25-50, 61-131 and 133-155 remain rejected under 35 U.S.C. §112, first paragraph for allegedly lacking enablement. Specifically, on page 2, section 2 of Paper No. 26, it is asserted that the specification is enabling for a polynucleotide encoding a

polypeptide of SEQ ID NO: 2, for polypeptides consisting of fragments of SEQ ID NO: 2, and for polynucleotides that specifically hybridize to a polynucleotide of SEQ ID NO: 1 as well as polynucleotides that encode polypeptides of SEQ ID NO: 2 in order to raise antibodies.

Preliminarily, Applicants note that claims 125 and 151 has been canceled without prejudice or disclaimer, thereby rendering the rejection moot with respect to these claims.

Further, in the interest of facilitating prosecution, and as agreed to in the Examiner Interview discussed above, claims 37, 41, 42, 76, 77, and 140 have been amended accordingly (*see* Paper No. 28). In view of these amendments, Applicants respectfully request reconsideration and withdrawal of the rejection with respect to these claims and any and all dependent claims therefrom.

However, it is also asserted in section 2 on page 2 of Paper No. 26 that the specification has failed to teach how to use other claimed polynucleotides (other than those used as hybridization probes or those that encode SEQ ID NO: 2 in order to raise antibodies). Further, it is also asserted in section 3, page 5 of Paper No. 26 that the specification allegedly fails to teach one of skill in the art which cell types to use to regulate cell differentiation and proliferation with the claimed invention as well as whether to use the claimed CRCGCL receptor to promote or inhibit cell differentiation and/or proliferation.

Applicants respectfully disagree and submit that in order to enable the claimed invention as required by 35 U.S.C. § 112, the specification need only enable a person of ordinary skill in the art to make the claimed polypeptides and practice a single use of the claimed polypeptides without undue experimentation. *See, e.g.,* M.P.E.P. § 2164.01(c).

This section of the MPEP also states that:

> When a compound or composition claim is limited by a particular use, enablement of that claim should be evaluated based on that limitation. See *In re Vaeck,* 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991).
> In contrast, when a compound or composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for nonenablement based on how to use. If multiple uses for claimed compounds or compositions are disclosed in the application, then an enablement rejection must include an explanation, sufficiently supported by the evidence, why the specification fails to enable each disclosed use. In other words, if any use is enabled when multiple uses are disclosed, the application is enabling for the claimed invention.

See MPEP §2164.01(c) at page 2100-175 to 176.

Applicants note that the Patent Office recognizes that it would be reasonable for the skilled artisan to use (1) the polynucleotides of SEQ ID NO: 1 as hybridization probes to detect activation of T-cells; and (2) the polypeptides of SEQ ID NO: 2 to raise antibodies useful for the detection and/or isolation of activated T-cells (see pages 2-3 of Paper No. 26). Accordingly, these multiple uses are reasonably correlated with the entire scope of the claimed invention, which according to the MPEP section above, is sufficient to preclude a rejection for nonenablement based on how to use.

Applicants also respectfully submit that the claimed polypeptides can also be used to transduce immune cell proliferation, as disclosed in the specification and as further supported by the executed Rule 132 Declarations of Dr. Paul Moore, submitted on February 27, 2001 and of Dr. Thi Sau Migone, submitted on February 8, 2002. For instance, the specification discloses and the Patent Office recognizes that the claimed CRCGCL receptor protein is homologous to the Interleukin-2 (IL-2) receptor common gamma chain (*see* page 7, line 24 to page 8, line 4 of the specification and pages 4-5 of Paper No. 26). The specification also teaches that, "cytokines that bind the IL-2 receptor common gamma chain, including IL-2, IL-4, IL-7, IL-9, and IL-15, are important for the growth and differentiation of immune cells, such as T and B lymphocytes, natural killer cells, macrophages, and monocytes." *See* page 1, lines 25-28 of the specification, emphasis added.

As a result, the specification expressly asserts as a specific, substantial and credible utility, that like the IL-2 common gamma chain, the claimed invention is useful for increasing the differentiation and proliferation of hematopoetic cells (see page 56, lines 18-22 of the specification). This assertion is reiterated on page 58, lines 33 to 36 in which the specification discloses, "CRCGCL polypeptides or polynucleotides can be used to treat or detect infectious agents. For example, by increasing the immune response, particularly increasing the proliferation and differentiation of B and/or T cells, infectious diseases may be treated." (Emphasis added).

The specification also asserts that the disclosed CRCGCL receptor proteins, particularly a soluble form of the full length receptor, are useful for reducing the activity of a membrane bound receptor by competing with it for free ligand (e.g., a cytokine). *See* page 45, lines 19-27 of the specification.

These assertions were understood by Dr. Migone, a skilled immunologist, as demonstrated in her Rule 132 Declaration submitted on February 8, 2002. For instance, in section 6 of her Declaration, Dr. Migone noted that the specification asserts that

because of the homology of the claimed invention to the Interleukin-2 receptor gamma chain and the various conserved domains contained within (i.e., the transmembrane domain, the WXWS domain, the Jak Box), she understood the disclosed CRCGCL receptor protein would be a cytokine receptor and be involved in the differentiation and proliferation of cells, just as the Interleukin-2 receptor gamma chain is. This understanding is supported by the fact that it was known in the art at the time of filing that the cytokines IL-2, IL-4, IL-7, IL-9, and IL-15 are all well-known T cell growth factors and that all these T cell growth factors use the IL-2 common gamma chain receptor. *See* section 7 of Dr. Migone's Rule 132 Declaration. Thus, considering the specification as a whole, coupled with the knowledge of a skilled artisan at the time of filing, Dr. Migone declares under oath that:

> An immunologist, after reading [the] statements made in the 626 Application and based upon what was known in the filed of cytokine research, would understand that the 626 Application is directed to the use of the CRCGCL receptor protein as a positive regulator of T cell proliferation and would also understand that the CRCGCL receptor protein antagonist is useful for inhibiting T cell proliferation... (*see* Declaration section 17, emphasis added).

Thus, it was reasonable to Dr. Migone, a skilled artisan, that since the claimed CRCGCL receptor protein is homologous to the IL-2 common gamma chain, like the IL-2 common gamma chain, the CRCGCL receptor protein would also function as a growth factor by positively regulating immune cell proliferation while an antagonist would function as an inhibitor of said proliferation.

This assertion that the disclosed CRCGCL protein is a cytokine receptor and its use as a transducer of proliferation was corroborated in the Rule 132 Declaration of Dr. Paul Moore submitted in February 27, 2001, in which data from a 293T reconstitution cell assay and flow cytometry indicate that CRCGCL binds a cytokine and activates the Jak-STAT signal transduction pathway. *See* sections 4 and 5 of Dr. Moore's Rule 132 Declaration. The data also shows that a soluble extracellular domain of CRCGCL also binds a cytokine and inhibits the Jak-STAT pathway. *See id.* at section 4. As disclosed in the specification, it was well known in the art that activation of the Jak-STAT pathway is indicative of proteins able to transduce cell proliferation, particularly of immune cells (*see, e.g.*, Example 13 at pages 85-88 of the specification; *see also* Leonard W.J. and O'Shea J.J., Jaks and STATs: biological implications, Annu. Rev. Innumol. 1998:16:293-322 (abstract only), submitted herewith as Exhibit D).

Thus, Dr. Moore's data clearly corroborates Applicants' assertions that the claimed CRCGCL receptor can transduce immune cell proliferation and that a soluble extracellular fragment is able to act as an antagonist of said proliferation.

The specification also clearly discloses the cell types upon which the claimed CRCGCL receptor polynucleotides would act upon, immune cells defined as hematopoetic cells, which include B and T cells. Applicants pointed out on page 6, line 8 of their last response dated July 22, 2002, the specification clearly asserts that the disclosed CRCGCL receptor protein acts to proliferate or differentiate immune cells, wherein immune cells are defined as cells that develop through a process called hematopoiesis, (*i.e.*, hematopoietic cells (*see* specification page 56, lines 19-21)), producing myeloid and lymphoid cells (*i.e.*, B and/or T cells (*see* specification page 58, lines 33-36)), from pluripotent stem cells (*see* specification page 56, lines 6-8).

Finally, as extensively discussed above, the specification clearly teaches that the disclosed CRCGCL receptor protein would act to positively regulate immune cell proliferation and differentiation, whereas an antagonistic form of the receptor, such as, for example, a soluble extracellular fragment, would inhibit. The Rule 132 Declaration of Dr. Migone submitted February 8, 2002 attests that as one skilled in the art, she would understand the present specification to disclose this assertion (*see* sections 6, 7, 10, 14, 15and 17 of Dr. Migone's Rule 132 Declaration). Yet, the Patent Office responds that this Dr. Migone's Declaration is not persuasive, stating:

> At pages 56-62 the specification simply makes generalized statements regarding any potential activity or the polypeptides toward any number of immune cell types. Statements such as "CRCGCL polynucleotides or polypeptides may have chemotaxis activity" Page 61 line 21, for example, do not provide the artisan with any particular knowledge, - only that the polypeptides might be tested for such activities.

(*See* page 6, lines 14-19 of Paper No. 26).

Applicants respectfully disagree and submit that the specification makes explicit assertions that the CRCGCL receptor protein will induce proliferation and/or differentiation, as discussed above, and as attested to by Dr. Migone in her Rule 132 Declaration. Further, the above-quoted statement, "CRCGCL polynucleotides or polypeptides may have chemotaxis activity" is simply one of the assertions of utility for the claimed invention. In fact, MPEP §2107.02 clearly states that:

> It is common and sensible for an applicant to identify several specific utilities for an invention, particularly where the invention is a product...However, regardless

> of the category of invention that is claimed (e.g., product or process), an applicant need only make one credible assertion of specific utility for the claimed invention to satisfy 35 U.S.C. §101 and 35 U.S.C. §112; additional statements of utility, even if not "credible," do not render the claimed invention lacking in utility.
>
> Statements made by the applicant in the specification or incident to prosecution of the application before the Office cannot, standing alone be the basis for a lack of utility rejection under 35 U.S.C. §101 or 35 U.S.C. §112.

Furthermore, Applicants submit that chemotaxis is a well-known biological activity exhibited by macrophages and leukocytes which attract and mobilize such cells to sites of inflammation, infection or hyperproliferation (*see* page 61, lines 20-37 of the specification). Chemotaxis is therefore a part of the immune response that includes proliferation and differentiation of immune cells and Applicants submit that such an assertion of utility does not undermine the specific, substantial and credible assertion that the CRCGCL receptor protein acts to transduce immune cell proliferation and differentiation and that antagonists can act to inhibit such activity. By finding Dr. Migone's Rule 132 Declaration unpersuasive in such a manner, Applicants submit that the Patent Office has failed to meet its burden in rebutting the evidence presented and arguments set forth, as proscribed by the MPEP § 716.01, regarding the sufficiency of submitted oaths or declarations:

> Where the evidence [in the declaration] is insufficient to overcome the rejection, the examiner must specifically explain why the evidence is insufficient. General statements such as "the declaration lacks technical validity" or "the evidence is not commensurate with the scope of the claims" without an explanation supporting such findings are insufficient.

Thus, Applicants respectfully request reconsideration of all of the evidence and arguments previously submitted to address this particular issue.

Thus, in view of the above, and as suggested during the Examiner Interview, claims 25, 34-36, 60, 140, and 154-155 have been amended in order to better define the claimed invention. Support for these amendments can be found throughout the specification as filed, as discussed above, therefore no new matter has been introduced. Applicants respectfully submit that according the requirements of MPEP § 2164.01(c) quoted above, the requirements of enablement should now be evaluated based upon what is now recited in the claims in conjunction with the evidence submitted previously as discussed above.

In further support of the enablement of the newly amended claims, the specification teaches biological assays to determine if the disclosed CRCGCL receptor protein proliferates immune cells (*see e.g.*, pages 88-89, Example 14; page 90, Example 15; pages 92-94, Example 17). The disclosed or otherwise known methods of making and screening polypeptides and fragments or variants thereof may be used to make and then determine, by routine experimentation, whether a given polypeptide encompassed by the claims is able to, for example, generate antagonists (including, but not limited to, for example, soluble fragments of CRCGCL) which would be useful in inhibiting the proliferation of immune cells, or to generate CRCGCL variants which could be useful in transducing immune cell proliferation. Applicants respectfully submit that such screening would not amount to undue experimentation. As provided for in the MPEP §2164.06(b):

> (B) In *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), the court reversed the rejection for lack of enablement under 35 U.S.C. §112, first paragraph, concluding that undue experimentation would not be required to practice the invention. The nature of monoclonal antibody technology is such that experiments first involve the entire attempt to make monoclonal hybridomas to determine which ones secrete antibody with the desired characteristics. The court found that the specification provided considerable direction and guidance on how to practice the claimed invention and presented working examples, that all of the methods needed to practice the invention were well known, and that there was a high level of skill in the art at the time the invention was filed. Furthermore, the applicant carried out the entire procedure for making a monoclonal antibody against HbsAg three times and each time was successful in producing at least one antibody which fell within the scope of the claims.

Applicants respectfully submit that the present situation is directly analogous to the facts presented in *In re Wands*. First, the present specification provides considerable direction and guidance on how to practice the claimed invention (*see* for example, page 17, lines 18-22, page 25, lines 12-36 of the specification on how to make fragments; page 10, line 34 to page 17, line 4 of the specification on how to make variants; *see also* page 17, lines 14-15; page 24, lines 9-16; page 25, lines 12-15 of the specification on how to use fragments of the invention; *see also* page 14, lines 23-32, and page 15, lines 7-15, and page 16, lines 21-27 of the specification on how to use variants).

Second, the present specification presents examples (*see e.g.*, Example 9, page 78 on how to make deletion mutants; pages 88-89, Example 14; page 90, Example 15; pages 92-94, Example 17) on how to test for proliferation and/or differentiation of T cells and myeloid cells. Furthermore, there was a high level of skill in the art at the time the invention was filed. Finally, Applicants carried out experiments for transducing immune

cell proliferation and demonstrated that the claimed invention binds a cytokine and promotes cell proliferation and that an extracellular soluble fragment could inhibit such proliferation. *See* Dr. Paul Moore's Rule 132 Declaration submitted February 27, 2001. Thus, Applicants respectfully submit that the claims are fully enabled.

Finally, on page 7 of Paper No. 26, the Patent Office alleges that the specification asserts that CRCGCL binds to cytokines but does not provide evidence to support the assertion, and that since IL-2R gamma (the closest homolog to CRCGCL) does not bind cytokine directly, CRCGCL, alone, would not be expected to regulate cell differentiation and/or proliferation, absent evidence to the contrary.

Applicants respectfully disagree with this interpretation of the teachings of the specification. This concern appears to be one of credibility of the assertion that the disclosed CRCGCL receptor protein can bind a cytokine alone, thus, Applicants will address this accordingly. It is well-settled Patent Office policy that applicants are entitled, when credibility of an assertion is challenged, to corroborate an assertion by submitting evidence to prove the truth of the assertion. This evidence is permitted to be post-filing. *See* In re Brana, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995).

On page 38, lines 1-27 of the specification, it is contemplated that the CRCGCL receptor protein polypeptides may be in the form of monomers or multimers, which encompasses homomers or heteromers. Thus, the invention contemplates both that the CRCGCL receptor protein can act alone or together with another polypeptide to exert is biological functions. Applicants submit that, while there are several examples in the art of multiple IL receptor subunit interactions being required for high affinity IL binding, the art recognizes that individual IL receptor subunits can, alone, bind ligand. For example, IL-3 can bind to *either* the IL-3Rα *or* IL-3Rβ subunits, *alone* (*see* Bona and Bonilla, Textbook of Immunology (submitted herewith as Exhibit A), p.194, line 1); IL-6 can bind the IL-6Rα chain, *alone*, or with the IL-6Rβ chain (*see* Bona and Bonilla, Textbook of Immunology, p.197, line 25); and IL-5 signaling through the IL-5R is predominantly through the β chain (*see* Bona and Bonilla, Textbook of Immunology, p.196, line 25). Thus, the assertion that CRCGCL can alone bind a cytokine would be reasonable to one of skill in the art. In fact, as described in section 5 of Paul Moore's Declaration submitted February 27, 2001, CRCGCL, was shown to bind a cytokine *alone*, as well as when co-transfected with the IL-7R alpha chain:

> In addition, flow cytometry was used to measure whether CRCGCL polypeptides bind a cytokine. A shift in the mean fluorescent intensity measured by FACScan on cells alone compared to cells treated with a ligand suggests that the ligand has associated with a cell surface molecule... As shift in the mean fluorescent intensity as measured by FACScan was detected when 293T cells transfected with CRCGCL **alone** and in **combination** with IL-7Rα chain were treated with FLAG-tagged TSLP. (Emphasis added).

Thus, Applicants respectfully submit that in view of the discussion above, the claims fully meet the enablement requirements of 35 U.S.C. § 112, first paragraph, and respectfully request that the rejection be reconsidered and withdrawn.

II. Rejections under 35 U.S.C. §112- Written Description

On page 9 of Paper No.26, claims 25-50, 60-131 and 133-155 remain rejected for an alleged lack of written description in the specification.

Applicants respectfully disagree, however, as discussed above, claims 125 and 151 has been canceled without prejudice or disclaimer, thereby rendering the rejection moot with respect to these claims.

Further, in the interest of facilitating prosecution, and as agreed to in the Examiner Interview discussed above, claims 37, 41, 42, 76, 77, and 140 have been amended accordingly (see Paper No. 28). In view of these amendments, Applicants respectfully request reconsideration and withdrawal of the rejection with respect to these claims and any and all dependent claims therefrom. Furthermore, as discussed above, claims 25, 34-36, 60, 140, and 154-155 have been amended in order to better define the claimed invention. Support for these amendments can be found throughout the specification as filed, as discussed above, therefore no new matter has been introduced.

The test for the written description requirement is whether one of ordinary skill in the art could reasonably conclude that the inventor has possession of the claimed invention in the specification as filed. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991); M.P.E.P. § 2163.02. Further, the Federal Circuit recently re-emphasized the well-settled principle of law that "[t]he written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [they] invented what is claimed,'" *Union Oil Co. v. Atlantic Richfield Co.*, 208 F.3d 989, 54 U.S.P.Q.2d 1227 (Fed. Cir. 2000). The court emphasized the importance of what the person of ordinary skill in the art would understand from

reading the specification, *rather than whether the specific embodiments had been explicitly described or exemplified.* Indeed, as the court noted, "the issue is whether one of skill in the art could derive the claimed ranges from the patent's disclosure." *Unocal*, 208 F.3d at 1001 (emphasis added). *See also Nelson v. Bowler*, 1 USPQ2d 2076, 2078-2079 (Bd. Pat. App. & Int'f 1986) ("[W]here the claims involved are drawn to specific compounds, it is well settled that it is not necessary for a party to expressly name the compounds to comply with the written description requirement ... The issue is whether the Nelson specifications convey clearly to those skilled in the art that Nelson invented the compounds at issue ...).

Applicants respectfully submit that the disclosure clearly contains written description support for the amended claims. For example, the present specification contemplates variants and fragments of the claimed invention (*see* for example, page 17, lines 18-22, page 25, lines 12-36 of the specification on fragments; page 10, line 34 to page 17, line 4 of the specification on variants). Furthermore, the specification contemplates specific fragments on page 17, line 34 to page 18, line 4 and on page 18, lines 5-14 and on page 24, lines 14-16 and Table 1.

Therefore, Applicants respectfully request that this rejection of the claims be reconsidered and withdrawn.

IV. Rejection under 35 U.S.C. §102

On page 10 of Paper No. 26, claims 140, 143, and 153 are rejected under 35 U.S. §102(b) as being allegedly anticipated by GenEmbl accession number X91553. This reference discloses a polynucleotide that comprises a nucleic acid that encodes the amino acid phenylalanine. It is asserted that:

> It is inherent feature of phenylalanine that it promotes (enhances) the proliferation of all animal cells (immune cells included) because it is an essential amino acid, see Lodish eds, Molecular Biology, page 193.

Preliminarily, Applicants note that claim 153 has been canceled and claim 140 has been amended, in accordance with the Examiner Interview, discussed above, thereby rendering the rejection with respect to the above claims moot. Accordingly, Applicants respectfully request that the rejection of claims 140, 143, and 153 under 35 U.S.C. §102(b) be withdrawn.

Nevertheless, with respect to the assertion above, Applicants respectfully disagree and traverse and submit that a prima facie case for anticipation has not been made because the cited reference does not support the scientific assertion made.

Applicants respectfully submit that the cited Lodish reference does not state that phenylalanine stimulates or promotes cell division, rather, it states that phenylalanine is an "essential" amino acid, meaning that the cell cannot produce the amino acid on its own, and therefore it must be obtained from the cell's environment in order to prevent the cell from dying. Therefore, it is unclear how the allegedly anticipating reference, GenEmbl accession number X91553, an EST, expressly or inherently teaches each and every element of the claimed invention.

Assuming arguendo, that a prima facie case for anticipation was made, Applicants respectfully submit the following evidence to rebut the scientific assertions made above. Applicants respectfully submit that preventing cell death is not the equivalent of promoting cell division. As stated on page 893 of Alberts *et al.* (submitted herewith as Exhibit B):

> ...for many decades all efforts to define the minimal requirements for cell proliferation failed; even in a medium containing all the obvious chemically defined nutrients, including glucose, amino acids, and vitamins, cells would only grow if the medium was supplemented with serum (emphasis added).

Cell proliferation, or division, requires the replication of cellular DNA, the segregation of replicated chromosomes into two separate cells, and usually a doubling of cell mass and duplication of cytoplasmic organelles (*see* Alberts *et al.* pages 863-866). These events are coordinated with one another during the cell cycle, of which M phase (mitotic phase), G1 phase (interval b/w completion of mitosis and beginning of DNA synthesis), S phase (replication of nuclear DNA), and G2 phase (interval b/w end of DNA synthesis and beginning of mitosis/M phase) are the traditional subdivisions. To promote or enhance cell proliferation is to stimulate cells out of a resting state (referred to as G0 phase) and into the cell cycle of division, or to increase the rate at which cells are dividing (i.e. entering and completing the cell cycle). To say that phenylalanine promotes cell proliferation is to say that it stimulates cells to divide, which according to the Alberts reference cited above, is not the case. Phenylalanine is only necessary for cells to stay alive (e.g., cell survival to avoid apoptosis).

Further, Applicants hereby submit pages taken from a Gibco-BRL catalog listing the various components included in a commercially available minimal essential medium

(MEM) (submitted herewith as Exhibit C). Phenylalanine is listed as an ingredient in MEM. It is well known in the art of tissue culture that MEM without the addition of serum is often used to "serum starve" tissue culture cells in order to synchronize them in a G0 phase prior to manipulation, as in for example, transient transfection techniques. The reason this can occur is that the lack of serum containing growth factors in the culture media will cause a gradual depletion of such factors necessary for proliferation. As these growth factors are depleted, cells will arrest their cell division and become quiescent, but not die since MEM contains nutrients such as vitamins and essential amino acids that are required for cell survival.

Furthermore, it has not been shown that the allegedly anticipating reference, GenEmbl accession number X91553, an EST, encodes a biologically relevant protein which, if introduced to immune cells, could either, by itself transduce proliferation of immune cells or that the phenylalanine residue encoded within the EST would be cleaved from its parent sequence in order to impose its alleged proliferative effects. Therefore, Applicants respectfully submit that neither the scientific statements made nor the reference cited support the rejection.

In view of the above comments, Applicants respectfully submit that GenEmbl Accession No. X91553 cannot anticipate, expressly or inherently, each and every element of the claimed invention. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection.

CONCLUSION

In view of the foregoing remarks, applicants believe that this application is now in condition for allowance. If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. §1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

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